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AGENCY: United States Patent and Trademark Office, GAU 1806

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DATE: April 15, 1998

RE: U.S.S.N. 08/779,767 (ALLIA.143A)
"COMPOUNDS, COMPOSITIONS AND METHODS FOR THE
ENDOCYTIC PRESENTATION OF IMMUNOSUPPRESSIVE FACTORS"

TOTAL # OF PAGES: 5, INCLUDING THIS COVER PAGE.

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M E M O R A N D U M

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DATE: April 15, 1998
 TO: Dr. Julie Reeves - Primary Examiner, Group 1806
 FROM: Chris Dayton - Patent Counsel, Alliance Pharmaceutical Corp.
 RE: Claims for Discussion at Interview - U.S.S.N. 08/779,767 (ALLIA.143A)
 Wednesday, April 22, 1998 at 1:00 PM

INFORMAL COMMUNICATION: DO NOT ENTER

Applicants are submitting the amended claims set forth below solely for the purpose of discussion at the above-referenced interview.

NON-WITHDRAWN INDEPENDENT CLAIMS FOR U.S.S.N 08/779,767:

1. (Amended) [An immunomodulating agent] An immunosuppressive compound for reducing an immune response in a vertebrate suffering from an immune disorder [for] by the endocytic presentation of [an immunosuppressive factor] a T cell receptor antagonist associated with class II MHC molecules on the surface of an antigen presenting cell of [a] said vertebrate [comprising] wherein the compound comprises at least [one Fc receptor ligand] an effective Fc receptor binding portion of a constant region of an immunoglobulin molecule and at least one [immunosuppressive factor] T cell receptor antagonist.

22. (Amended) A pharmaceutical composition for reducing an immune response in a vertebrate suffering from an immune disorder by the endocytic presentation of [an immunosuppressive factor] a T cell receptor antagonist associated with class II MHC molecules on the surface of an antigen presenting cell of [a] said vertebrate the composition comprising at least one [immunomodulating agent] immunosuppressive compound and a pharmaceutically acceptable carrier, said at least one [immunomodulating agent] immunosuppressive compound comprising at least [one Fc receptor ligand] an effective Fc receptor binding portion of a constant region of an immunoglobulin molecule and at least one [immunosuppressive factor] T cell receptor antagonist.

T cell?
B cell?
Component?

Said...
auto immune?
T cell?
leukemia?

Ph P only.

pharmaceutically acceptable carrier

SELECTED TERMS DISCUSSED IN THE INSTANT OFFICIAL ACTION:

Immunosuppressive Factor: Deleted in the proposed claims.

Immunomodulating Agent: Deleted in the proposed claims.

Fc Receptor Ligand: Deleted in the proposed claims.

Analog: Extensive support in the paragraph bridging pages 19 & 20. Propose filing 132 Declaration.

Antibody/Antigen Complex: Support at page 21, lines 9-11. Comprises a immunoglobulin molecule sterically bound to a T cell receptor antagonist.

CDR's: T cell receptor may be inserted or replace CDR region(s). Support at page 24, lines 15-28 and Examples 2, and 6-12. Disruption of antigen binding site in such constructs irrelevant for purposes of claimed invention as long as Fc binding intact.

Chimeric: Extensive support in the paragraph bridging pages 21 & 22. Propose filing 132 Declaration.

SCHEMATIC REPRESENTATION:

A schematic representation of a preferred embodiment of the present invention and hypothetical mechanism in accordance with the teachings of the instant application are attached for review.

Among the salient points to be derived from the representation are:

1. The invention comprises peripheral regulation of activated mature T cells only. Thymic modulation of T cells is essentially irrelevant for the purpose of practicing the present invention.
2. Conservation of antigen binding site in chimeric immunoglobulins used in accordance with the present invention is irrelevant as uptake and endocytic presentation is mediated by Fc receptor binding. As long the constant region derived from the incorporated immunoglobulin is capable of effectively binding the Fc receptor, the associated T cell receptor antagonist will be efficiently presented.
3. The present invention does not depend in any way on the administration of an MHC molecule or part thereof.
4. The present invention is not directed to immunization of a subject but rather to the induction of anergy through the competitive T cell receptor binding of MHC class II complexes associated with an endocytically derived T cell receptor antagonist.

102/103 CITED ART DISTINGUISHED:*naturally occurring*

Applicant submits that the cited art may be briefly be distinguished as follows:

Kuchroo et al.: Peptide ligands only. No suggestion of Fc mediated uptake. Essentially cumulative with respect to WO 96/16086 as discussed on page 9, lines 25 et seq.

Mueller et al.: Peptide ligands only, although teach human administration. No suggestion of Fc mediated uptake. Again, essentially cumulative with respect to WO 96/16086.

WO94/14847, Zanetti et al.: Teach IgG constructs comprising microbial peptides. No suggestion regarding administration of T cell receptor antagonists.

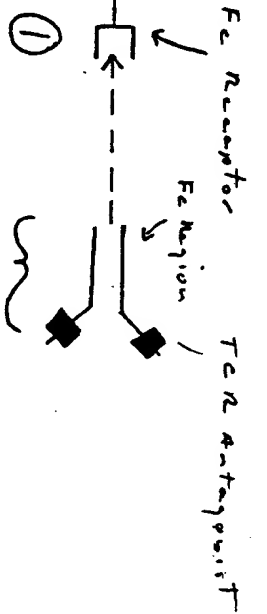
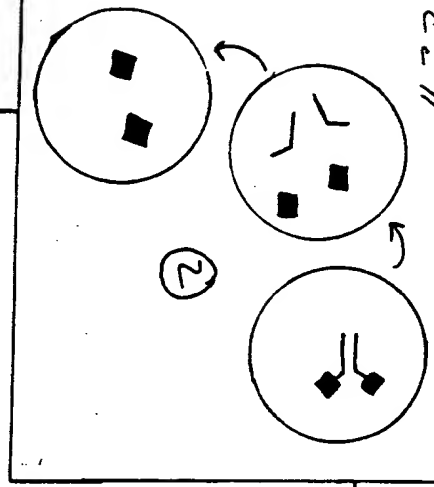
5,508,386, Zanetti et al.: Largely cumulative with respect to WO94/14847. No suggestion that incorporated epitope could comprise T cell receptor antagonists.

Kappler et al.: Only teaches constructs comprising MHC for competition binding. No indication that Fc mediated uptake could be used to present the selected peptide antigen.

Selick et al.: Teaches the use of soluble constructs comprising a MHC component. No suggestion of Fc mediated uptake or presentation of T cell receptor antagonists.

Bona et al.: Review article. Similar to Zanetti et al. above. Fails to teach or suggest the use of T cell receptor antagonists.

Antigen Presenting Cell (page 17-18)



- ① Immunosuppressive Compound binds to Fc Receptor + is Endocytosed
- ② Endocytosed Compound is enzymatically degraded to Free TCR Antagonist
- ③ TCR Antagonist, associated with MHC Class II, binds to T Cell Receptor + Presented
- ④ Antagonist-MHC Complex binds to T Cell Receptor but does NOT activate Inflammation Cascade

